SURGICAL TOOLS AND TECHNIQUES FOR STIMULATION

CROSS-REFERENCES TO RELATED APPLICATIONS

This application claims priority from US Provisional Patent Application 60/426,180, filed November 14, 2002, entitled, "Surgical tools and techniques for stimulation," which is assigned to the assignee of the present application and is incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates generally to medical procedures and electronic devices. More specifically, the invention relates to the use of electrical devices for implantation in the head and surgical techniques for implanting the devices.

BACKGROUND OF THE INVENTION

The blood-brain barrier (BBB) is a unique feature of the central nervous system (CNS), which isolates the brain from the systemic blood circulation. To maintain the homeostasis of the CNS, the BBB prevents access to the brain for many substances circulating in the blood.

The BBB is formed by a complex cellular system of endothelial cells, astroglia, pericytes, perivascular macrophages, and a basal lamina. Compared to other tissues, brain endothelia have the most intimate cell-to-cell connections: endothelial cells adhere strongly to each other, forming structures specific to the CNS called "tight junctions" or zonula occludens. They involve two opposing plasma membranes, which form a membrane fusion with cytoplasmic densities on either side. These tight junctions prevent cell migration or cell movement between endothelial cells. A continuous uniform basement membrane surrounds the brain capillaries. This basal lamina encloses contractile cells called pericytes, which form an intermittent layer and probably play some role in phagocytosis activity and defense if the BBB is breached. Astrocytic end feet, which cover the brain capillaries, build a continuous sleeve and maintain the integrity of the BBB by the synthesis and secretion of soluble growth factors (e.g., gamma-glutamyl transpeptidase) essential for the endothelial cells to develop their BBB characteristics.

Because of the BBB, certain non-surgical treatments of the brain based upon systemic introduction of compounds through the bloodstream have been ineffective or

less effective. For example, chemotherapy has been relatively ineffective in the treatment of CNS metastases of systemic cancers (e.g., breast cancer, small cell lung cancer, lymphoma, and germ cell tumors) despite clinical regression and even complete remission of these tumors in non-CNS systemic locations. The most important factors determining drug delivery from blood into the CNS are lipid solubility, molecular mass, and electrical charge. A good correlation exists between the lipid solubility of a drug, expressed as the octanol/water partition coefficient, and the drug's ability to penetrate or diffuse across the BBB. This is particularly relevant for drugs with molecular weights smaller than 600 Dalton (Da). The normal BBB prevents the passage of ionized water soluble drugs with molecular weight greater than 180 Da. Most currently available effective chemotherapeutic agents, however, have a molecular weight between 200 and 1200 Da. Therefore, based both on their lipid solubilities and molecular masses, the passage of many agents is impeded by the BBB.

In addition to transcellular diffusion of lipophilic agents, there are several specific transport mechanisms to carry certain molecules across the brain's endothelial cells. Specific transport proteins exist for required molecules, such as glucose and amino acids. Additionally, absorptive endocytosis and transcytosis occur for cationized plasma proteins. Specific receptors for certain proteins, such as transferrin and insulin, mediate endocytosis and transport across the cell.

Non-surgical treatment of neurological disorders is generally limited to systemic introduction of compounds such as neuropharmaceuticals and other neurologically active agents that might remedy or modify neurologically related activities and disorders. Such treatment is limited, however, by the relatively small number of known compounds that pass through the BBB. Even those that do cross the BBB often produce adverse reactions in other parts of the body or in non-targeted regions of the brain.

There have been a number of different studies regarding efforts to cross the BBB, specifically with regard to overcoming the limited access of drugs to the brain. Such efforts have included, for example, chemical modification, development of more hydrophobic analogs, or linking an active compound to a specific carrier. Transient opening of the BBB in humans has been achieved by intracarotid infusion of hypertonic mannitol solutions or bradykinin analogs. Also, modulation of the P-glycoprotein, whose substrates are actively pumped out of brain cells into capillary lumens, has been found to facilitate the delivery of drugs to the brain.

The sphenopalatine ganglion (SPG) is a neuronal center located in the brain behind the nose. It consists of parasympathetic neurons innervating the middle cerebral and anterior cerebral lumens, the facial skin blood vessels, and the lacrimal glands. Activation of this ganglion is believed to cause vasodilation of these vessels. A second effect of such stimulation is the opening of pores in the vessel walls, causing plasma protein extravasation (PPE). This effect allows better transport of molecules from within these blood vessels to surrounding tissue.

The middle and anterior cerebral arteries provide the majority of the blood supply to the cerebral hemispheres, including the frontal and parietal lobes in their entirety, the insula and the limbic system, and significant portions of the following structures: the temporal lobes, internal capsule, basal ganglia and thalamus. These structures are involved in many of the neurological and psychiatric diseases of the brain. Currently the SPG is a target of manipulation in clinical medicine, mostly in attempted treatments of severe headaches, such as cluster headaches. The ganglion is blocked either on a short-term basis, by applying lidocaine, or permanently, by ablation with a radio frequency probe. In both cases the approach is through the nostrils.

The following references, which are incorporated herein by reference, may be useful:

Delepine, L., Aubineau, P., "Plasma protein extravasation induced in the rat dura mater by stimulation of the parasympathetic sphenopalatine ganglion," Experimental Neurology, 147, 389-400 (1997).

Hara, H., Zhang, Q. J., Kuroyanagi, T., Kobayashi, S., "Parasympathetic cerebrovascular innervation: An anterograde tracing from the sphenopalatine ganglion in the rat," Neurosurgery, 32, 822-827 (1993).

Jolliet-Raint, P., Tillement, J. P., "Drug transfer across the blood-brain barrier and improvement of brain delivery," Fundam. Clin. Pharmacol., 13, 16-25 (1999).

Kroll, R. A., Neuwelt, E. A., "Outwitting the blood brain barrier for therapeutic purposes: Osmotic opening and other means," Neurosurgery, 42, 1083-1100 (1998).

Sanders, M., Zuurmond, W. W., "Efficacy of sphenopalatine ganglion blockade in 66 patients suffering from cluster headache: A 12-70 month follow-up evaluation," Journal of Neurosurgery, 87, 876-880 (1997).

Seylaz, J., Hara, H., Pinard, E., Mraovitch, S., MacKenzie, E. T., Edvinsson, L, "Effects of stimulation of the sphenopalatine ganglion on cortical blood flow in the rat," Journal of Cerebral Blood Flow and Metabolism, 8, 875-878 (1988).

Van de Waterbeemd, H., Camenisch, G., Folkers, G., Chretien, J. R., Raevsky, O. A., "Estimation of blood brain barrier crossing of drugs using molecular size and shape and h bonding descriptors," Journal of Drug Targeting, 6, 151-165 (1998).

Suzuki, N., Hardebo, J. E., Kahrstrom, J., Owman, C., "Selective electrical stimulation of postganglionic cerebrovascular parasympathetic nerve fibers originating from the sphenopalatine ganglion enhances cortical blood flow in the rat," Journal of Cerebral Blood Flow and Metabolism, 10, 383-391 (1990).

Suzuki, N., Hardebo, J. E., Kahrstrom, J., Owman, C. H., "Effect on cortical blood flow of electrical stimulation of trigeminal cerebrovascular nerve fibres in the rat," Acta Physiol. Scand., 138, 307-315 (1990).

Branston NM, "The physiology of the cerebrovascular parasympathetic innervation," British Journal of Neurosurgery 9:319-329 (1995).

Branston NM et al., "Contribution of cerebrovascular parasympathetic and sensory innervation to the short-term control of blood flow in rat cerebral cortex," J Cereb Blood Flow Metab 15(3):525-31 (1995).

Toda N et al., "Cerebral vasodilation induced by stimulation of the pterygopalatine ganglion and greater petrosal nerve in anesthetized monkeys," Neuroscience 96(2):393-398 (2000).

Seylaz J et al., "Effect of stimulation of the sphenopalatine ganglion on cortical blood flow in the rat," J Cereb Blood Flow Metab 8(6):875-8 (1988).

PCT Patent Publication WO 01/85094 to Shalev and Gross, which is assigned to the assignee of the present patent application and whose disclosure is incorporated herein by reference, describes methods and apparatus for stimulating the sphenopalatine ganglion to modify properties of the blood brain barrier and cerebral blood flow for the treatment of medical conditions. Treatment is accomplished directly via stimulation of the sphenopalatine ganglion and/or indirectly by the facilitation of drug transport across the blood brain barrier via stimulation of the sphenopalatine ganglion.

US Patent 6,526,318 to Ansarinia and related PCT Patent Publication WO 01/97905 to Ansarinia, whose disclosure is incorporated herein by reference, describes a method for treating a patient by placing at least one electrode on or proximate to at least one of the patient's sphenopalatine ganglia, sphenopalatine nerves, or vidian nerves, and activating the electrode to apply an electrical signal and/or a medical solution to at least one of those ganglia or nerves. The '318 patent and '905 publication also describe surgical techniques for implanting the electrode via a coronoid notch of the patient.

U.S. Patent 6,405,079 to Ansarinia, whose disclosure is incorporated herein by reference, describes methods for treating medical conditions by implanting one or more electrodes in regions of the sinus and applying electrical stimulation and/or medical solutions to the implantation site. The '079 patent also describes surgical techniques for implanting the electrode.

SUMMARY OF THE INVENTION

In some embodiments of the present invention, apparatus for stimulating the "sphenopalatine ganglion (SPG) system," as defined hereinbelow, is surgically implanted so as to stimulate the SPG system. Typically, the surgical procedure is performed in a relatively minimally-invasive manner to reduce patient discomfort during and after the procedure. Once implanted, the apparatus typically delivers the energy to the SPG system in order to control and/or modify SPG-related behavior, e.g., in order to induce changes in cerebral blood flow and/or to modulate permeability of the blood-brain-barrier (BBB). These embodiments may be used in many medical applications, such as, by way of illustration and not limitation, (a) the treatment of cerebrovascular disorders such as stroke, (b) the treatment of migraine headaches, (c) the treatment of Alzheimer's disease, (d) the facilitation of drug transport across the BBB, and/or (e) the facilitation of extraction of analytes from the brain.

In the present patent application, including the claims, "SPG system" means the SPG and associated neuroanatomical structures, including neural tracts originating in or reaching the SPG, including outgoing and incoming parasympathetic and sympathetic tracts, which tracts include preganglionic fibers of the SPG (fibers contained within the vidian nerve) and postganglionic fibers of the SPG (fibers that travel anterogradely from the SPG toward the brain vascular bed, including the anterior and posterior ethmoidal

nerves, and including the retro-orbital branches of the SPG, which are fibers that connect the SPG with orbital neural structures).

It is to be appreciated that, in general, the techniques described herein may be applied directly, or applied with changes *mutatis mutandis*, so as to facilitate stimulation of one or more of the following and thereby facilitate treatment of a medical condition:

- a sphenopalatine ganglion (SPG) (also called a pterygopalatine ganglion);
- an anterior ethmoidal nerve;
- a posterior ethmoidal nerve;
- a communicating branch between the anterior ethmoidal nerve and the SPG (retro-orbital branch);
- a communicating branch between the posterior ethmoidal nerve and the SPG (retro-orbital branch)
- a nerve of the pterygoid canal (also called a vidian nerve), such as a greater superficial petrosal nerve (a preganglionic parasympathetic nerve) or a lesser deep petrosal nerve (a postganglionic sympathetic nerve);
- a greater palatine nerve;
- a lesser palatine nerve;
- a sphenopalatine nerve;
- a communicating branch between the maxillary nerve and the sphenopalatine ganglion;
- a nasopalatine nerve;
- a posterior nasal nerve;
- an infraorbital nerve;
- an otic ganglion;
- an afferent fiber going into the otic ganglion; and/or
- an efferent fiber going out of the otic ganglion.

According to some embodiments of the present invention, a method and apparatus are provided to facilitate placement of at least one electrode adjacent to the SPG via an endoscopic transpalatine approach to the SPG. Typically, local anesthetic is applied to the oral palatine mucosa and a greater palatine block is performed prior to a mucoperiosteal incision proximate the greater palatine foramen to reveal the contents of the foramen. A trocar comprising a flexible guide tube is typically inserted vertically through the incision to provide access for endoscopic dissection and visualization tools, which are used for the subsequent portion of the procedure. Typically, the endoscopic tools are used for subperiosteal dissection to detach the greater palatine canal contents from the osseous part of the canal and provide access to the vidian foramen and a portion of the SPG.

Typically, at least one electrode is placed next to or in contact with the SPG via the flexible guide tube. In an embodiment, each electrode is flat so as to provide a large contact area between the electrode and SPG. Typically, the electrode is flexible enough to be rolled up and inserted through the trocar and guide tube and sufficiently elastic to resume a generally planar shape once through the trocar and guide tube. Additionally or alternatively, the electrode has a curved shape such that it may be hooked around a nerve in the SPG system, such as the vidian nerve.

Typically, the at least one electrode comprises two or more electrodes, driven to operate in a multi-polar mode (e.g., in a bipolar mode for the case of two electrodes).

According to some embodiments of the present invention, a method and apparatus are provided to facilitate placement of at least one electrode adjacent to the SPG via a transpalatine approach to the SPG. The area of the greater palatine foramen is anesthetized, and a full-thickness mucogingival incision is performed at the midline of the hard palate, including about 0.5 cm of the soft palate. Two releasing incisions are performed at the ends of the midline incision. A mucoperiosteal flap is raised, and the greater palatine neurovascular bundle is carefully exposed, revealing the contents of the greater palatine foramen. A stylet is inserted posteriorly through the greater palatine canal to the greater palatine neurovascular bundle, and supported against the posterior wall of the greater palatine canal. The stylet is removed, and a series of passive tip periosteal elevators, having successively greater distal shaft diameters, is used to widen the path created using the stylet.

An introducer is provided for introducing a neural stimulator into the greater palatine canal. The introducer typically comprises a handle for manipulating the introducer, a rod, and a protective sleeve. The neural stimulator typically comprises an electrode support, a receiver, and a connecting tube. The electrode support is mounted on the introducer by fitting the protective sleeve of the introducer over the electrode support. During the surgical procedure, after the greater palatine canal has been widened, the introducer is inserted into the greater palatine canal, and a surface of the stimulator that comprises at least one electrode is placed in contact with the posterior aspect of the sphenopalatine ganglion.

Subsequent to placement of the at least one electrode, proper placement is typically assured by running a test current through the at least one electrode and monitoring the physiological effect on the patient. Typically, once proper placement of the at least one electrode is assured, the at least one electrode is coupled to a control unit. For some applications, the control unit is implanted in the patient. Alternatively, an external control unit is used to control the at least one electrode.

According to some embodiments of the present invention, a method and apparatus are provided to facilitate placement of at least one electrode adjacent to the SPG via a combined trans-maxillary sinus and trans-nasal endoscopic assisted approach. Typically, after administration of appropriate anesthesia, the posterior wall of the maxillary sinus is carefully dissected and the anterior part of the sphenopalatine fossa is dissected via a trans-maxillary approach. The dissection is typically performed approximately 0.5 mm from the medial wall of the maxillary sinus, under direct endoscopic visualization. Subsequently, a complete nasal endoscopic examination is typically performed on both sides, and then, under direct visualization, an incision is made about 0.4 mm - about 0.8 mm under the second conchae on the operating side. Typically, a mucoperiosteal flap is raised posteriorly and inferiorly, to allow the sphenopalatine artery to be dissected and clamped. The sphenopalatine fossa is then typically approached under direct endoscopic visualization, and the lateral wall of the nose is penetrated. Subsequently, in an embodiment, the SPG is approached via the maxillary sinus. In another embodiment, the SPG is accessed via a trans-nasal approach.

Typically, an introducer, comprising a hollow tube, is inserted through the dissected tissue to provide a pathway for introduction of the at least one electrode, which comprises a lead wire, to a region adjacent to the SPG. In an embodiment the electrodes

are flat, such that a large surface area is available for contact with the SPG. In another embodiment, one or more of the electrodes are curved, so as to wrap around a portion of a nerve such as the vidian nerve, or another nerve in the SPG system.

Once the at least one electrode is placed, a controlled stimulation is typically performed by passing a current through the lead wire to the electrode to confirm that the electrode is properly placed. Evaluation of the proper placement of the at least one electrode comprises one or more of: (1) evaluating the vasodilatation of blood vessels in the eye, (2) assessment of cerebral blood flow by using a transcranial Doppler, (3) assessment of forehead perfusion by using Laser Doppler, and (4) assessment of forehead perfusion by a temperature sensor. In an embodiment, once proper placement of the electrodes has been verified, the electrodes are coupled to an implantable control unit. In another embodiment, the electrodes are coupled to an external control unit by wired or wireless means.

There is therefore provided, in accordance with an embodiment of the present invention, apparatus for treating a subject, including:

a stimulation device, adapted to be implanted in a vicinity of a site selected from the list consisting of: a sphenopalatine ganglion (SPG) of the subject and a neural tract originating in or leading to the SPG; and

a connecting element, coupled to the stimulation device, and adapted to be passed through at least a portion of a greater palatine canal of the subject.

In an embodiment, the portion of the greater palatine canal has a length of at least about 2 cm, and the connecting element is adapted to be passed through the portion.

In an embodiment, the connecting element includes at least one mark, adapted to indicate a depth of insertion of the stimulation device in the greater palatine canal.

In an embodiment, the stimulation device is adapted to stimulate the site, and to configure the stimulation to be sufficient to induce a change in cerebral blood flow of the subject.

In an embodiment, the stimulation device is adapted to stimulate the site, and to configure the stimulation to be sufficient to modulate permeability of a blood-brain-barrier of the subject.

In an embodiment, the site includes the SPG of the subject, and the stimulation device is adapted to be implanted in the vicinity of the SPG.

In an embodiment, the site includes a vidian nerve of the subject, and the stimulation device is adapted to be implanted in the vicinity of the vidian nerve.

In an embodiment, the site includes an ethmoidal nerve of the subject, and the stimulation device is adapted to be implanted in the vicinity of the ethmoidal nerve.

In an embodiment, the site includes a retro-orbital branch of the SPG of the subject, and the stimulation device is adapted to be implanted in the vicinity of the retro-orbital branch.

In an embodiment, the apparatus includes an introducer, adapted for mounting the stimulation device thereon, and to be passed through the at least a portion of the greater palatine canal.

In an embodiment, the stimulation device includes at least one electrode. For example, the electrode may be configured to wrap around a nerve of the subject in the vicinity of the site..

In an embodiment, the apparatus includes a stimulator, coupled to the connecting element, and adapted to be fixed to a hard palate of the subject. For example, the stimulator may be adapted to be coupled to the hard palate in a supraperiosteal region thereof. For some applications, the stimulator is adapted to be coupled to an upper surface of the hard palate in a nasal cavity of the subject. For some applications, the stimulator is adapted to be coupled to a lower surface of the hard palate.

There is further provided, in accordance with an embodiment of the present invention, apparatus for insertion into a greater palatine canal of a subject, including a stylet, which includes:

a proximal rod shaft, having a first diameter; and

a distal rod shaft, having a second diameter less than the first diameter, such that a region between the proximal rod shaft and the distal rod shaft is shaped so as to define a shoulder which is adapted to prevent insertion of the distal rod shaft into a sphenopalatine fossa of the subject beyond a depth of the greater palatine canal.

In an embodiment, the distal rod shaft includes a cutting implement, located in a vicinity of a distal tip of the shaft.

In an embodiment, the proximal rod shaft has a length of between about 20 mm and about 150 mm.

In an embodiment, the first diameter is between about 1.5 mm and about 6 mm.

In an embodiment, the distal rod shaft has a length of between about 3 mm and about 20 mm.

In an embodiment, the second diameter is between about 1 mm and about 1.5 mm.

In an embodiment, the apparatus includes a periosteal elevator for insertion into the greater palatine canal, the elevator including at least one mark adapted to indicate a depth of insertion of the periosteal elevator in the greater palatine canal.

There is still further provided, in accordance with an embodiment of the present invention, apparatus for insertion into a greater palatine canal of a subject, including a periosteal elevator, which includes at least one mark adapted to indicate a depth of insertion of the periosteal elevator in the greater palatine canal.

There is also provided, in accordance with an embodiment of the present invention, a method for implanting a treatment stimulation device in a vicinity of a site of a subject, including:

passing the device through a greater palatine foramen of the subject; and

bringing the device into contact with the vicinity of the site, the site selected from the list consisting of: a sphenopalatine ganglion (SPG) of the subject and a neural tract originating in or leading to the SPG.

There is also provided, in accordance with an embodiment of the present invention, a method for implanting a treatment stimulation device in a vicinity of a site of a subject, including:

passing the device through at least a portion of a greater palatine canal of the subject; and

bringing the device into contact with the vicinity of the site, the site selected from the list consisting of: a sphenopalatine ganglion (SPG) of the subject and a neural tract originating in or leading to the SPG.

For some applications, the site includes the SPG of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the vicinity of the SPG.

For some applications, the site includes a vidian nerve of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the vicinity of the vidian nerve.

For some applications, the site includes an ethmoidal nerve of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the vicinity of the ethmoidal nerve.

For some applications, the site includes a retro-orbital branch of the SPG of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the retro-orbital branch.

For some applications, bringing the device into contact includes:

applying stimulation with the device;

observing one or more physiological responses of the subject to the stimulation; and

verifying desired placement of the device responsive to the observation.

For some applications, bringing the device into contact includes applying stimulation with the device, and configuring the stimulation to be sufficient to induce a change in cerebral blood flow of the subject. For some applications, bringing the device into contact includes applying stimulation with the device, and configuring the stimulation to be sufficient to modulate permeability of a blood-brain-barrier of the subject.

For some applications, the stimulation device includes at least one electrode, and bringing the device into contact includes bringing the electrode into contact with the vicinity of the site. For some applications, bringing the electrode into contact includes wrapping the electrode around a nerve of the subject in the vicinity of the site.

For some applications, the stimulation device includes a stimulator, the method including fixing the stimulator to a hard palate of the subject. For example, fixing the stimulator to the hard palate may include coupling the stimulator to a supraperiosteal region of the hard palate. In an embodiment, fixing the stimulator to the hard palate includes coupling the stimulator to an upper surface of the hard palate in a nasal cavity of

the subject. In an embodiment, fixing the stimulator to the hard palate includes coupling the stimulator to a lower surface of the hard palate.

In an embodiment, passing the device through the greater palatine foramen includes determining a depth of insertion of the device in a greater palatine canal of the subject by observing at least one mark on the device indicative of the depth of the insertion.

In an embodiment, passing the device through the greater palatine foramen includes widening a greater palatine canal of the subject using a series of periosteal elevators having successively greater diameters.

In an embodiment, passing the device through the greater palatine foramen includes widening a greater palatine canal of the subject using a series of tools having successively greater diameters.

In an embodiment, passing the device through the greater palatine foramen includes mounting the device on an introducer, and passing the introducer through the greater palatine foramen.

In an embodiment, passing the device through the portion of the greater palatine canal includes determining a depth of insertion of the device in the greater palatine canal by observing at least one mark on the device indicative of the depth of the insertion.

In an embodiment, passing the device through the at least a portion of the greater palatine canal includes passing the device through at least about 2 cm of the greater palatine canal.

In an embodiment, passing the device through the at least a portion of the greater palatine canal includes widening the portion using a series of periosteal elevators having successively greater diameters.

In an embodiment, passing the device through the at least a portion of the greater palatine canal includes widening the portion using a series of tools having successively greater diameters.

In an embodiment, passing the device through the at least a portion of the greater palatine canal includes mounting the device on an introducer, and passing the introducer through the portion.

There is yet additionally provided, in accordance with an embodiment of the present invention, a method for implanting a treatment device in a vicinity of a site of a subject, including:

passing the device through a trans-maxillary sinus of the subject; and

bringing the device into contact with the vicinity of the site, the site selected from the list consisting of: a sphenopalatine ganglion (SPG) of the subject and a neural tract originating in or leading to the SPG.

In an embodiment, the site includes the SPG of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the vicinity of the SPG.

In an embodiment, the site includes a vidian nerve of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the vicinity of the vidian nerve.

In an embodiment, the site includes an ethmoidal nerve of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the vicinity of the ethmoidal nerve.

In an embodiment, the site includes a retro-orbital branch of the SPG of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the retro-orbital branch.

In an embodiment, bringing the device into contact includes:

applying stimulation with the device;

observing one or more physiological responses of the subject to the stimulation; and

verifying desired placement of the device responsive to the observation.

There is still additionally provided, in accordance with an embodiment of the present invention, a method for implanting a treatment device in a vicinity of a site of a subject, including:

passing the device through a sphenopalatine foramen canal of the subject; and

bringing the device into contact with the vicinity of the site, the site selected from the list consisting of: a sphenopalatine ganglion (SPG) of the subject and a neural tract originating in or leading to the SPG.

In an embodiment, the site includes the SPG of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the vicinity of the SPG.

In an embodiment, the site includes a vidian nerve of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the vicinity of the vidian nerve.

In an embodiment, the site includes an ethmoidal nerve of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the vicinity of the ethmoidal nerve.

In an embodiment, the site includes a retro-orbital branch of the SPG of the subject, and bringing the device into contact with the vicinity of the site includes bringing the device into contact with the retro-orbital branch.

In an embodiment, bringing the device into contact includes:

applying stimulation with the device;

observing one or more physiological responses of the subject to the stimulation; and

verifying desired placement of the device responsive to the observation.

There is also provided, in accordance with an embodiment of the present invention, a method for implanting a treatment device in a vicinity of an ethmoidal nerve of a subject, including:

passing the device through an ethmoidal foramen of the subject; and

bringing the device into contact with the vicinity of the ethmoidal nerve.

In an embodiment, the ethmoidal nerve includes an anterior ethmoidal nerve of the subject, and bringing the device into contact includes bringing the device into contract with the vicinity of the anterior ethmoidal nerve.

In an embodiment, the ethmoidal nerve includes a posterior ethmoidal nerve of the subject, and bringing the device into contact includes bringing the device into contract with the vicinity of the posterior ethmoidal nerve.

In an embodiment, bringing the device into contact includes:

applying stimulation with the device;

observing one or more physiological responses of the subject to the stimulation; and

verifying desired placement of the device responsive to the observation.

The present invention will be more fully understood from the following detailed description of the embodiments thereof, taken together with the drawings in which:

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a pictorial illustration of the roof of the oral cavity, showing a site for an incision, in accordance with an embodiment of the present invention;

Fig. 2 is a schematic illustration of endoscopic apparatus for accessing the sphenopalatine ganglion (SPG) system, in accordance with an embodiment of the present invention;

Fig. 3 is a pictorial illustration of an endoscopic tool accessing the SPG system, in accordance with an embodiment of the present invention;

Figs. 4A and 4B are schematic illustrations of an electrode introducer for placing an electrode in the SPG system, in accordance with an embodiment of the present invention;

Figs. 5A, 5B, and 5C are schematic illustrations of electrode supports to be placed in the SPG system, in accordance with embodiments of the present invention;

Fig. 6 is a schematic illustration of an electrode to be hooked around a nerve in the SPG system, in accordance with an embodiment of the present invention;

Fig. 7 is a schematic illustration of an endoscopic tool for placing an electrode in the SPG system, in accordance with an embodiment of the present invention;

Fig. 8 is a schematic illustration of a system for supporting electrical leads during placement of an electrode in the SPG system, in accordance with an embodiment of the present invention;

Figs. 9A and 9B are schematic, partially sectional illustrations of receivers for receiving control and power signals to drive an electrode that is placed in the SPG system, in accordance with embodiments of the present invention;

Fig. 10 is a schematic, sectional illustration of the placement of an electrode in the SPG system and a control unit on the upper jaw, in accordance with an embodiment of the present invention;

Fig. 11 is a schematic, pictorial illustration of the placement of an electrode adjacent to the anterior ethmoidal nerve and a control unit on the orbital rim, in accordance with an embodiment of the present invention;

Fig. 12 is a schematic, pictorial illustration showing incisions in a roof of an oral cavity and associated anatomical structures, in accordance with an embodiment of the present invention;

Fig. 13 is a schematic illustration of a stylet, in accordance with an embodiment of the present invention;

Fig. 14 is a schematic, pictorial illustration of a posterolateral roof of an oral cavity, in accordance with an embodiment of the present invention;

Figs. 15A and 15B are schematic illustrations of a passive tip periosteal elevator used to widen the path created using the stylet of Fig. 13, in accordance with embodiments of the present invention;

Fig. 16 is a schematic illustration of an implantable neural stimulator, in accordance with an embodiment of the present invention;

Fig. 17 shows an electrode configuration for use with an electrode support of the stimulator of Fig. 16, in accordance with an embodiment of the present invention;

Fig. 18 is a schematic illustration of an electrode introducer, in accordance with an embodiment of the present invention;

Fig. 19 is a schematic illustration of the stimulator of Fig. 16 mounted on the electrode introducer of Fig. 18, in accordance with an embodiment of the present invention; and

Fig. 20 is a schematic, sectional illustration of the placement of an electrode in the SPG system and a control unit on the upper jaw, in accordance with an embodiment of the present invention.

DETAILED DESCRIPTION OF EMBODIMENTS

Fig. 1 is a schematic, pictorial illustration showing a roof of an oral cavity 20 and associated anatomical structures, where dissection commences in a surgical procedure to access the sphenopalatine ganglion (SPG) system, in accordance with an embodiment of the present invention. In this embodiment, soft tissue is dissected to expose a greater palatine foramen 22, in order to allow access via the greater palatine canal (also known as the pterygopalatine canal) to the SPG system by means of an endoscopic transpalatine approach.

To start the procedure, the patient is typically positioned with an open mouth, and a topical and local anesthetic is applied to the oral palatine mucosa. Typically, after the local anesthetic has taken the desired effect (typically after about 2 - 3 minutes), a greater palatine nerve block is performed. Greater palatine foramen 22 is then located, typically by the anatomical landmark of a second upper molar 24. Typically, a mucoperiosteal incision is made in front of the location of greater palatine foramen 22, and the contents of the foramen are dissected and revealed.

Fig. 2 is a schematic illustration showing endoscopic apparatus 30, which is used in the surgical procedure to access the SPG once the contents of greater palatine foramen 22 have been dissected and revealed, in accordance with an embodiment of the present invention. Apparatus 30 comprises a handle 38, which contains a keyhole opening 42, through which a flexible hollow sleeve 36 is placed. Typically sleeve 36 serves as a conduit and guide for introduction of endoscopic tools, while handle 38 is used to move and orient sleeve 36 and any introduced endoscopic tools. Further typically, sleeve 36 comprises a slit 43, running the length of the sleeve, which is lined up with keyhole opening 42, such that handle 38 and sleeve 36 can be removed from around wires subsequently introduced through the sleeve.

In some embodiments of the present invention, hollow sleeve 36 is adapted to permit a flexible shaft 34 to be introduced and advanced to a desired operative site. Flexible shaft 34 is typically adapted such that a surgical tool 40 may be attached to the distal end of the shaft. For example, Fig. 2 shows a surgical tool comprising a periosteal elevator. In some embodiments of the present invention, flexible shaft 34 is hollow so as to allow the introduction of additional apparatus to the operative site. Fig. 2 shows an embodiment in which a trocar 32 is introduced through hollow flexible shaft 34.

Typically, endoscopic apparatus 30 is used to proceed with the surgical procedure subsequent to dissection of the contents of the greater palatine foramen, by inserting hollow sleeve 36 into the greater palatine foramen with the aid of handle 38. Once the hollow sleeve is suitably positioned, flexible shaft 34 with attached surgical tool 40 and trocar 32 are typically inserted through hollow sleeve 36. In an embodiment, surgical tool 40 comprises a periosteal elevator. Trocar 32 is typically advanced using a gentle 180 degree axial rotation, and subperiosteal dissection is performed with the aide of surgical tool 40 so as to detach the contents of the greater palatine canal from the osseous portion of the canal. Typically, the dissection is monitored with endoscopic visualization, while irrigation and suction are used as necessary to maintain the site of dissection. Trocar 32 should typically be introduced about 2 centimeters relative to the bony entrance of the greater palatine canal, with allowable variation for the anatomy of individual patients.

Fig. 3 illustrates shaft 34 and the anatomy of the pterygopalatine fossa 50, which shows an SPG 52 adjacent to a sphenopalatine artery 54, in accordance with an embodiment of the present invention. The pterygopalatine fossa is a bilateral intraosseous space at the craniofacial junction. Because of its location, it is considered together with the structures of the paranasal sinuses. The fossa resembles a four-sided pyramid with an imaginary base, anterior, posterior and medial wall all converging at the vertex. The base corresponds to the region of the orbital vertex. The anterior wall is bordered by a small vertical portion of the maxillary tuberosity close to its junction with the palatine vertical plate. The medial wall is formed by the vertical plate of the palatine bone and is crossed by the sphenopalatine foramen. The posterior wall corresponds to the anterior face of the pterygoid process of the sphenoid bone. The lateral wall lies against the skull, sealed by fibrous tissue, and allows the passage of the vascular and nervous structures. The vertex of the pyramid is the junction of the walls, where the palatine osseous canals connect the pterygopalatine fossa with the oral cavity through the hard palate.

A vidian nerve 57, contained in a vidian foramen 56, is seen to be connected to SPG 52. Typically, the vidian foramen and nerve are approached under direct endoscopic visualization, after the steps described hereinabove with reference to Fig. 2. Typically, hollow flexible shaft 34 (see also Fig. 2) is introduced towards vidian nerve 57 and/or SPG 52.

Fig. 4A shows an electrode introducer 60, comprising a flexible rod 62, to which an electrode support 58 is attached, and a handle 64 for manipulating the introducer, in

accordance with an embodiment of the present invention. Typically, electrode support 58 is introduced to the region of the vidian nerve and the SPG via flexible shaft 34.

Fig. 4B shows flexible electrode support 58, rolled to fit inside shaft 34, at a point in time as support 58 is advanced out from shaft 34, such that support 58 opens upon exiting the distal end of shaft 34, in accordance with an embodiment of the present invention. Electrodes, such as plate electrodes 66a, described hereinbelow with reference to Fig. 5A, are affixed to one or more sites on the electrode support, and are positioned to be in contact with a target site such as the SPG when the support unrolls.

Figs. 5A, 5B, and 5C show several electrode configurations for use with electrode support 58, in accordance with respective embodiments of the present invention. The three illustrated electrode configurations are typically flat, providing a relatively large surface area for contact with the SPG or other tissue. Additionally, the flexibility and flat thin shapes of the electrode support and the electrodes are conducive to being rolled up, for some applications, so as to fit through flexible shaft 34 and subsequently return to essentially their initial flat shape (see Fig. 4B). Fig. 5A shows a simple plate electrode design comprising two plate electrodes 66a, which are each connected to respective leads 65, typically but not necessarily by laser welding. Other embodiments comprise more than two plate electrodes 66a. Typically, plate electrodes 66a comprise platinum/iridium or other suitable substances known in the art of tissue stimulation.

Fig. 5B shows an alternate electrode design where each of two compound plate electrodes 66b typically comprises a horizontal strip 67, to which a plurality of vertical plates 69 is coupled. Typically, each horizontal strip 67 is coupled to a respective lead 65 by laser welding. Horizontal strip 67 and vertical plates 69 typically comprise platinum/iridium or other suitable substances known in the art of tissue stimulation.

Fig. 5C shows another electrode design providing a large surface area for contact with the SPG, comprising two shaped electrodes 66c, which are shaped to provide the desired electrical stimulation to the SPG. In an embodiment, electrodes 66c are formed by cutting the shapes out of a simple plate comprising platinum/iridium or other suitable substances known in the art of tissue stimulation.

For some applications, electrode support 58 shown in Figs. 5A, 5B, and 5C is about 4 mm by about 6-10 mm. The total contact surface area between the SPG (or other

tissue) and the electrodes in the embodiments shown in these figures is, for some applications, between about 0.5 mm^2 and about 2 mm^2.

Fig. 6 shows an electrode 68 that is configured to wrap around a nerve, in accordance with an embodiment of the present invention. Electrode 68 is shown in the figure in a bipolar configuration, for placement at respective longitudinal sites on the nerve. For some applications, electrode 68 comprises a single monopolar "hook" electrode. Typically, electrode 68 comprises two conductive strips 70, pre-bent to a curved shape such that they can be placed during a procedure to wrap around a target nerve, for example the vidian or ethmoidal nerves. The inner portion of conductive strips 70 is designated to be in contact with the target nerve (or only slightly separated therefrom), and provides the electrical stimulation to the nerve. The outer surfaces of strips 70, i.e., those surfaces not in contact with the nerve, are typically sheathed or otherwise coated in a non-conductive material 72, to reduce or eliminate stimulation of tissues surrounding the target nerve.

Fig. 7 shows details of flexible rod 62 (see Figs. 4A and 4B), which is used in the placement of electrode support 58 and comprises one or more electrical leads 74 for transmitting electrical power to the electrodes (e.g., electrodes 66a, 66b, or 66c) on electrode support 58, in accordance with an embodiment of the present invention. Typically, electrical leads 74 are cast into a solid elastomer sheathing 76 to provide a desired degree of flexibility and strength during the introduction of the electrodes, and to also provide the isolation of the leads from bodily tissues and fluids.

Fig. 8 shows apparatus for supporting and protecting electrical leads 74 while maintaining sufficient strength and flexibility, in accordance with an embodiment of the present invention. Typically, leads 74 are threaded through a hollow tube 80, chosen to provide appropriate strength and flexibility, which typically comprises a plurality of supports 82 along the length of tube 80 for holding leads 74 and preventing damage to the leads during introduction or operation of the electrodes.

Fig. 9A shows a partially sectional view of a receiver 78, which is adapted to be coupled to the proximal end of rod 62 (Fig. 4A) by a base 92 and to receive power and control signals from a control unit that drives electrodes, such as electrodes 66a, 66b, or 66c, on electrode support 58, in accordance with an embodiment of the present invention. Receiver 78 comprises a coil 90 and an electronics pod 94, which are coupled to a base 92

and adapted to receive power and drive the electrodes. Typically, coil 90 is constructed using Drawn Filled Tube technology, and typically comprises a combination of MP35N and silver. In an embodiment, coil 90 is adapted to receive control and power inputs wirelessly. By way of example but not limitation, RF electromagnetic fields and/or oscillating magnetic fields are used to wirelessly power and control the electrodes via coil 90 and electronics pod 94.

Fig. 9B shows a partially sectional view of a receiver 100, which is adapted to be coupled to the proximal end of rod 62 (Fig. 4A) by a base 92 and to receive power and control signals from a control unit that drives electrodes, such as electrodes 66a, 66b, or 66c, on electrode support 58, in accordance with an embodiment of the present invention. Receiver 100 comprises an electronics module 102, which comprises a plurality of connectors 104 for wired connections to a typically non-implanted control unit.

Typically, receivers 78 and 100 are coated with a non-permeable coating such as, but not limited to, Parylene, which isolates the receiver from physiological fluids and tissues. Further typically, the receivers are encased in a relatively pliant layer such as an elastomer, which serves as an outer casing for the receiver.

Alternatively or additionally, techniques are used that are described in US Provisional Patent Application 60/426,182, filed November 14, 2002, entitled, "Stimulation circuitry and control of electronic medical device," which is assigned to the assignee of the present application and is incorporated herein by reference.

Typically, once electrode support 58 is properly placed, endoscopic device 30 (see Fig. 2) is removed from the patient, and receiver 78 or receiver 100 remains in the patient, typically immediately above or below the hard palate or at the ridge of the eye, and is connected by leads to the electrodes on electrode support 58. Note that keyhole opening 42 in hollow sleeve 36 and slit 43 in handle 38 allow for the removal of these items without affecting leads 74, because the leads pass through the keyhole and slit as the handle and sleeve are removed. Alternatively, sleeve 36 is made so as to split along its length prior to removal.

Fig. 10 shows the placement of electrode support 58 adjacent to SPG 52 and the placement of a stimulator 112 comprising receiver 78 in the supraperiosteal region of the hard palate of the patient, typically at midline, in accordance with an embodiment of the present invention. Alternatively, stimulator 112 is implanted in the nasal cavity on the

upper surface of the hard palate. Typically, stimulator 112 receives power wirelessly from an external control unit temporarily placed in or near the mouth. Stimulator 112 is typically fixed to the hard palate with microscrews. Alternatively, the control unit powers and controls stimulator 112 by a wired connection between the control unit and a receiver 100 (Fig. 9B) incorporated into the stimulator. Further alternatively, one or more lead wires are brought out through the skin and coupled to an external control unit.

Typically, but not necessarily, techniques described in PCT Patent Publication WO 01/85094 to Shalev and Gross, entitled, "Method and apparatus for stimulating the sphenopalatine ganglion to modify properties of the BBB and cerebral blood flow," or the US national phase application thereof, US Patent Application 10/258,714, filed October 25, 2002, both of which are assigned to the assignee of the present patent application and incorporated herein by reference, are adapted for use with the techniques of these embodiments of the present invention. In particular, electrodes implanted adjacent to the SPG, using the relatively minimally-invasive surgical techniques and associated surgical tools of the present invention, are driven by a stimulator (e.g. control unit), using control and driving circuitry and treatment protocols described therein, to control the blood brain barrier and/or treat neurological symptoms or disease.

In an embodiment of the present invention, a combined trans-maxillary sinus and trans-nasal endoscopic-assisted approach to the SPG is used in order to implant at least one electrode in a region of the SPG. Typically, to start the procedure, the patient is given a local and topical anesthesia in the intraoral vestibulum at the area of the canine fossa, and a topical intranasal anesthesia at the region of the lateral nasal wall of the operated side. The posterior wall of the maxillary sinus is typically dissected, and the anterior part of the sphenopalatine fossa is dissected via a trans-maxillary approach. Typically, the dissection is performed approximately 0.5 mm from the medial wall of the maxillary sinus under direct endoscopic visualization.

Typically, a complete nasal endoscopic examination is performed on both sides and then under direct visualization an incision is made about 0.4 – about 0.8 mm under the second conchae on the operating side. A mucoperiosteal flap is typically raised posteriorly and inferiorly followed by dissection and clamping of the sphenopalatine artery. Subsequently, under direct visualization, the lateral wall of the nose is typically penetrated and the sphenopalatine fossa is approached. In an embodiment of the present invention, the surgeon now approaches the SPG via the trans-maxillary sinus. In another

embodiment, the surgeon approaches the SPG via the trans-nasal approach. The specific approach is typically dependent on the anatomical topography of the patient.

At this stage of the procedure, endoscopic device 30 (see Fig. 2) is typically inserted in the dissected tissue and used to place an electrode adjacent to the SPG, as discussed hereinabove for the endoscopic transpalatine approach to the SPG.

Yet another embodiment of the present invention comprises an upper blepharoplasty approach to the anterior and/or posterior ethmoidal nerves, in order to implant at least one electrode adjacent to the anterior and/or posterior ethmoidal nerves. Typically, to start the procedure, the patient's upper and lower eyelids are sterilized. A local anesthetic is typically applied to the upper eyelid. Once the anesthetic has taken effect, an incision in the skin following an eyelid crest is typically performed. In an embodiment, the incision is approximately 15 mm long.

Once the skin has been dissected, the orbicularis muscle is typically passed through by performing a blunt dissection. Subsequently, a sharp incision of the periosteum, typically about 15 mm in length, is made on the superomedial aspect of the orbit. Typically, the subperiosteal tissue is then dissected to expose the anterior ethmoidal foramen and its contents, including the anterior ethmoidal nerve. Alternatively or additionally, the dissection is performed so as to expose the posterior ethmoidal nerve. Once the anterior and/or posterior ethmoidal nerve has been exposed, at least one electrode is implanted adjacent to the nerve.

Fig. 11 shows the placement of an electrode 120 adjacent to the posterior ethmoidal nerve 124 in the region of an orbital cavity 128, in accordance with an embodiment of the present invention. Typically, electrode 120 is coupled to a stimulator 122 by a lead 130. Stimulator 122 is typically fixed to the superior orbital rim. Following placement of electrode 120, lead 130, and stimulator 122, incisions in the periosteum, muscle and skin are closed with standard surgical techniques.

Alternatively, electrode 120 is placed adjacent to an anterior ethmoidal nerve 126. Further alternatively, a plurality of electrodes 120 is placed so as to stimulate both the anterior and the posterior ethmoidal nerves.

Typically, verification and/or optimization of the electrode nerve interface after the electrodes are placed is performed by observing the effects of stimulation on one or more physiological responses. Potential observations include, but are not limited to: (1)

evaluating the vasodilatation of blood vessels of the eye, (2) assessment of cerebral blood flow by using trans-cranial Doppler, (3) assessment of forehead perfusion by using Laser-Doppler, and (4) assessment of forehead perfusion by a temperature sensor.

Fig. 12 is a schematic, pictorial illustration showing incisions 200 in a roof of oral cavity 20 and associated anatomical structures, where dissection commences in a surgical procedure to access the SPG system, in accordance with an embodiment of the present invention. In this embodiment, soft tissue is dissected to expose greater palatine foramen 22 (see Fig. 1), in order to allow access via the greater palatine canal to the SPG system by means of a transpalatine approach.

Prior to beginning the surgical procedure, the patient is typically instructed to rinse his mouth with an antimicrobial oral rinse, such as 0.2% chlorhexidine solution, for at least about five minutes. For some patients, the surgical procedure is performed under general anesthesia. To begin the procedure, the patient is typically positioned with an open mouth (typically using a mouth gag). Greater palatine foramen 22 (Fig. 1) is then located, typically by the anatomical landmark of second upper molar 24. (Greater palatine foramen 22 is typically located 1 cm medial to second upper molar 24 at the border between the hard and the soft palates.) The area of greater palatine foramen 22 is anesthetized, such as by 2 ml lidocaine. A full-thickness about 3 cm mucogingival incision 210 is made at the midline of the hard palate, including about 0.5 cm of the soft palate. Two releasing incisions 212, about 1 cm each, are made at the ends of midline incision 210. Typically, electrosurgery is used to make these releasing incisions in order to minimize bleeding. A mucoperiosteal flap 214 is raised, and the greater palatine neurovascular bundle is carefully exposed, typically using Jeter cleft palate scissors and a periosteal elevator, such as an Obwegeser periosteal elevator. The neuromuscular bundle is typically preserved using a molt curette. Mucoperiosteal flap 214 is gently and firmly retracted using a flap retractor, such as a Jensen flap retractor, revealing the contents of greater palatine foramen 22.

Fig. 13 is a schematic illustration of a stylet 240, which is the first instrument to be inserted into the greater palatine canal once the contents of greater palatine foramen 22 have been dissected and revealed, in accordance with an embodiment of the present invention. Stylet 240 comprises a handle 242 and a rod 244 coupled to the handle, such as with a screw (screw not shown). Rod 244 comprises a proximal rod shaft 246 and a narrower distal rod shaft 248. Proximal rod shaft 246 typically has a length L_1 of

between about 20 mm and about 150 mm, such as about 88 mm or about 100 mm, and a diameter of between about 1.5 mm and about 6 mm, such as about 4 mm or about 4.6 mm. Distal rod shaft 248 typically has a length L_2 of between about 3 mm and about 20 mm, such as about 10 mm or about 12 mm, and a diameter of between about 1 mm and about 1.5 mm, such as about 1.3 mm. A distal tip of distal rod shaft 248 typically comprises a cutting implement 249, such as a blade. Typically, rod 244 is shaped so as to define a shoulder 250 between proximal rod shaft 246 and distal rod shaft 248. Shoulder 250 is adapted to prevent insertion of distal rod shaft 248 into the sphenopalatine fossa beyond the depth of the greater palatine canal.

Fig. 14 is a schematic, pictorial illustration of a posterolateral roof 280 of oral cavity 20 (Fig. 1), in accordance with an embodiment of the present invention. Shown in the figure are greater palatine foramen 22, a greater palatine canal 282, and a posterior wall 284 of greater palatine canal 282. During the surgical procedure, stylet 240 is inserted posteriorly through the greater palatine canal to the greater palatine neurovascular bundle, and supported against posterior wall 284. Stylet 240 is pushed vertically using a gentle plus and minus 45-degree clockwise and counterclockwise rotational motion, until shoulder 250 of stylet 240 (Fig. 13) reaches the exposed entrance to greater palatine foramen 22 (at the roof of the mouth) .

Figs. 15A and 15B are schematic illustrations of a passive tip periosteal elevator 300 used to widen the path created using stylet 240, in accordance with embodiments of the present invention. Passive tip periosteal elevator 300 comprises a handle 310 and a rod 312 coupled to the handle, such as with a screw (screw not shown). Rod 312 comprises a proximal rod shaft 314 and a distal rod shaft 316, a distal tip 318 of which is typically rounded. Proximal rod shaft 314 typically has a length L_3 of between about 30 mm and about 150 mm, such as about 70 mm or about 100 mm, and a diameter of between about 2 mm and about 6 mm, such as about 4 mm or about 4.6 mm. Distal rod shaft 316 typically has a length L_4 of between about 15 mm and about 50 mm, such as about 30 mm or about 40 mm, and a diameter of between about 1 mm and about 2 mm. Typically, passive tip periosteal elevators having certain distal rod shaft 248 diameters (such as between about 1 mm and about 1.4 mm) have a rounded distal rod shaft (configuration not shown in figures), while passive tip periosteal elevators having other distal rod shaft 248 diameters (such as greater than about 1.4 mm) have a distal rod shaft with at least one flattened surface 320, as shown in the figures. Optionally, flattened

surface 320 is shaped to define file-like slots 322, having a depth of about 0.2 mm, for example.

For some applications, distal rod shaft 316 is straight, as shown in Fig. 15A, while for other applications, distal rod shaft 316 is bent, as shown in Fig. 15B. Such a bend is typically located between about 3 mm and about 10 mm, such as about 4 mm, from distal tip 318, and typically has an angle between about 5 degrees and about 15 degrees, such as about 10 degrees.

During the surgical procedure, after stylet 240 has been removed, a series of passive tip periosteal elevators 300, having successively greater distal rod shaft 316 diameters, is typically used to widen the path created using stylet 240. First, the narrowest passive tip periosteal elevator of the series (e.g., having a distal rod shaft 316 diameter of about 1 mm) is introduced through the path created by stylet 240, keeping tight contact between the instrument and posterior wall 284 of greater palatine canal 282. This insertion is typically performed with a plus and minus 45-degree clockwise and counterclockwise rotational motion and gentle abrading maneuver. If using a passive tip periosteal elevator having a flattened surface, as described hereinabove, the flattened surface is typically used for the abrading maneuver. The passive tip periosteal elevator is typically inserted into the greater palatine canal to a depth of about 25 mm. Alternatively, the depth of the greater palatine canal is measured prior to or during the implantation procedure, in which case the tip is inserted to the measured depth. Typically, the depth of insertion is indicated on the elevator by one or more marks 324 on distal rod shaft 316.

The first, narrowest, passive tip periosteal elevator is removed, and this widening step of the surgical procedure is repeated using elevators having successively wider distal rod shaft diameters, until greater palatine canal 282 is widened, typically, to about 2 mm. Generally, irrigation and suction are performed between periosteal elevator replacements in order to remove osseous debris.

Fig. 16 is a schematic illustration of an implantable neural stimulator 350, in accordance with an embodiment of the present invention. Stimulator 350 comprises an electrode support 352, a receiver 354, and a connecting element 356, such as a connecting tube. (Other suitable structures for connecting element 356 will be apparent to one of ordinary skill in the art, having read the disclosure of the present patent application.) Electrode support 352 comprises one or more electrodes 358, positioned on an electrode

surface 360 of the support, such that the electrodes are in contact with a target site (e.g., the SPG) when stimulator 350 is implanted. For some applications, electrodes 358 are arranged in the electrode configuration described hereinbelow with reference to Fig. 17. Alternatively, for other applications, electrodes 358 are arranged in one of the electrode configurations described hereinabove with reference to Figs. 5A, 5B, or 5C. Receiver 354 receives power and control signals from a control unit that drives electrodes 358. For some applications, receiver 354 is similar to receiver 78 or receiver 100, described hereinabove with reference to Fig. 9A and Fig. 9B, respectively. Alternatively, other suitable configurations are utilized. Optionally, connecting element 356 comprises one or more marks 362 that indicate the depth of insertion of stimulator 350 into the greater palatine canal.

Fig. 17 shows an electrode configuration for use with electrode support 352, in accordance with an embodiment of the present invention. In this configuration, electrode support 352 comprises two insulated regions: an insulated shaft region 370 and an insulated tip region 372. Electrodes 358 comprise an annular electrode 374 and a rod electrode 376, electrically isolated from one another by insulated tip region 372.

Fig. 18 is a schematic illustration of an electrode introducer 400, in accordance with an embodiment of the present invention. Introducer 400 is used for introducing stimulator 350 into the greater palatine canal. Introducer 400 typically comprises a handle 402 for manipulating the introducer, a rod 404, to which electrode support 352 (Fig. 16) is attached, and a protective sleeve 406.

Fig. 19 is a schematic illustration (not necessarily to scale) of stimulator 350 mounted on electrode introducer 400, in accordance with an embodiment of the present invention. Stimulator 350 is mounted on electrode introducer 400 by inserting electrode support 352 into protective sleeve 406.

During the surgical procedure, after greater palatine canal 282 has been widened, electrode introducer 400 is inserted into greater palatine canal 282, typically to depth of about 25 mm. Alternatively, the depth of the greater palatine canal is measured prior to or during the implantation procedure, in which case the introducer is inserted to the measured depth. If connecting element 356 comprises marks 362, as described hereinabove with reference to Fig. 16, such marks are typically used to determine the depth of the introducer. Typically, electrode surface 360 of stimulator 350 is placed in

contact with the posterior aspect of the SPG. Mucoperiosteal flap 214 (Fig. 12) is sutured over receiver 354, which is located flush with the palatine bone, typically using forceps, such as Adson forceps, and a needle holder.

Fig. 20 shows the placement of electrode support 352 posteriorly adjacent to SPG 52 and the placement of a stimulator 380 comprising receiver 354 in the supraperiosteal region of the hard palate of the patient, typically at midline, in accordance with an embodiment of the present invention. Alternatively, stimulator 112 is implanted in the nasal cavity on the upper surface of the hard palate. Typically, stimulator 380 receives power wirelessly from an external control unit temporarily placed in or near the mouth. Stimulator 380 is typically fixed to the hard palate with microscrews. Further alternatively, one or more lead wires are brought out through the skin and coupled to an external control unit. Still further alternatively, stimulator 380 is battery powered, and comprises control circuitry to allow it to operate independently of outside control.

In some embodiments, techniques described herein are practiced in combination with techniques described in one or both of the following co-assigned US applications: (i) US Patent Application 10/294,310, filed November 14, 2002, and a corresponding PCT application claiming priority therefrom, filed on even date herewith, entitled, "Stimulation for treating eye pathologies," and (ii) US Provisional Patent Application 60/426,182, filed November 14, 2002, entitled, "Stimulation circuitry and control of electronic medical device." All of these applications are incorporated herein by reference.

Techniques described in this application may be practiced in combination with methods and apparatus described in one or more of the following patent applications, which are assigned to the assignee of the present patent application and are incorporated herein by reference:

- US Patent Application 10/258,714, filed October 25, 2002, entitled, "Method and apparatus for stimulating the sphenopalatine ganglion to modify properties of the BBB and cerebral blood flow," or the above-referenced PCT Publication WO 01/85094
- US Provisional Patent Application 60/364,451, filed March 15, 2002, entitled, "Applications of stimulating the sphenopalatine ganglion (SPG)"
- US Provisional Patent Application 60/368,657, filed March 28, 2002, entitled, "SPG Stimulation"

- US Provisional Patent Application 60/376,048, filed April 25, 2002, entitled, "Methods and apparatus for modifying properties of the BBB and cerebral circulation by using the neuroexcitatory and/or neuroinhibitory effects of odorants on nerves in the head"
- US Provisional Patent Application 60/388,931, filed June 14, 2002, entitled "Methods and systems for management of Alzheimer's disease"
- US Provisional Patent Application 60/400,167, filed July 31, 2002, entitled, "Delivering compounds to the brain by modifying properties of the BBB and cerebral circulation"
- US Provisional Patent Application 60/426,180, filed November 14, 2002, entitled, "Surgical tools and techniques for sphenopalatine ganglion stimulation"
- US Provisional Patent Application 60/426,182, filed November 14, 2002, entitled, "Stimulation circuitry and control of electronic medical device"
- US Patent Application 10/294,310, filed November 14, 2002, entitled, "SPG stimulation for treating eye pathologies"
- US Patent Application US 10/294,343, filed November 14, 2002, and a corresponding PCT application claiming priority therefrom, filed on even date herewith, entitled, "Administration of anti-inflammatory drugs into the CNS"
- US Provisional Patent Application 60/426,181, filed November 14, 2002, entitled, "Stimulation for treating ear pathologies"
- US Provisional Patent Application 60/448,807, filed February 20, 2003, entitled, "Stimulation for treating autoimmune-related disorders of the CNS"
- US Provisional Patent Application 60/461,232 to Gross et al., filed April 8, 2003, entitled, "Treating abnormal conditions of the mind and body by modifying properties of the blood-brain barrier and cephalic blood flow"
- a PCT Patent Application to Shalev, filed April 25, 2003, entitled, "Methods and apparatus for modifying properties of the BBB and cerebral

circulation by using the neuroexcitatory and/or neuroinhibitory effects of odorants on nerves in the head"

- a US provisional patent application, filed September 26, 2003, entitled, "Diagnostic applications of stimulation"
- a US patent application, filed October 2, 2003, entitled, "Targeted release of nitric oxide in the brain circulation for opening the BBB"
- a PCT patent application, filed on even date herewith, entitled, "Stimulation circuitry and control of electronic medical device"
- a PCT patent application, filed on even date herewith, entitled, "Stimulation for treating ear pathologies"

It is noted that the figures depicting embodiments of the present invention are not necessarily drawn to scale, and, instead, may change certain dimensions in order to more clearly demonstrate some aspects of the invention.

It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather, the scope of the present invention includes both combinations and subcombinations of the various features described hereinabove, as well as variations and modifications thereof that are not in the prior art, which would occur to persons skilled in the art upon reading the foregoing description.